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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,388	01/10/2001	Juha Punnonen	0154.310US	2485

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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/760,388	Punnonen et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 10, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-35, 37-42, 44-68, and 70-78* is/are pending in the application.

4a) Of the above, claim(s) *1-32, 42, 44-51, 60-67, 77, and 78* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *33-35, 37-41, 52-59, 68, 70-76* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election of Group III, Claims 33-35, 37-41, 52-59, 68, and 70-76, with traverse, is acknowledged. Applicant traverses the restriction in that it requires restriction within claims. Applicant further argues that the examiner has made no *prima facie* case showing a serious search burden. In particular Groups I-III, V, and VI all fall in Class 435.

These arguments not found persuasive for the following reasons. Regarding restriction within individual claims, said restriction is proper when multiple inventions are recited in individual claims. Applying the logic of Applicant's argument, Claim 1 of any application need only recite all of the inventions of any application to make restriction impossible. Regarding search burden, while it has been noted that the Groups are classified in the same class, in the establishment of search burden, classification of subject matter is merely one indication of the burdensome nature of the search involved. In the biotechnological arts, the literature searches are generally far more important in evaluating burden of search. In the instant application, the claimed inventions consist of different products, e.g., the dendritic cells of Group III versus the T cells of Group VI, and different methods, e.g., the method of producing an antigen presenting cell of Group I versus the method of inducing an immune response of Group VII. Clearly, different searches and different issues are involved in the examination of each group, thus search burden has been established.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-32, 42, 44-51, 60-67, and 77-78 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 33-35, 37-41, 52-59, 68, and 70-76 are being acted upon.

3. The disclosure is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. See, for example, page 32 of the specification. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 57, 70, and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) The term "a target cell of an autoimmune response" in Claim 57 is vague and indefinite as the term is not defined in the specification. Accordingly, the metes and bounds of precisely which cells would be encompassed by the claim cannot be determined.

B) The phrase "altered cytokine profile" in Claim 70 is vague and indefinite as the phrase is not defined in the specification. Accordingly, the metes and bounds of precisely which cells would be encompassed by the claim cannot be determined.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 57 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of "a target cell of an autoimmune response". The specification fails to define or disclose any such cells. Given the definition of well-known terms such as "amino acid sequence" and "epitope" in the jumbo specification,

the provision of said definitions demonstrating Applicant's acknowledgment of the necessity of describing the claimed invention with reasonable clarity, it is curious that a critical, and certainly less readily understood, limitation of a claim is not defined. One of skill in the art must therefore conclude then that the specification fails to disclose an adequate written description or a representative number of species to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

8. Claims 58, 59, 68, and 70-76 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed vaccine could function for its intended purpose for the treatment or prevention of essentially all known pathogen-induced diseases, as well as cancers and autoimmune diseases.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

It is noted that whereas the specification discloses the details of a number of routine tasks it only vaguely discloses the use of the vaccine of the instant claims. Accordingly, it is again curious that Applicant should see the need to describe, in detail, methods which would be expected to work, i.e., isolating a dendritic cell, yet only vaguely discloses highly complex methods such as *in vivo* treatment or prevention of highly diverse diseases/conditions, which would be expected to be unpredictable.

Additionally, what little disclosure is provided seems somewhat contradictory, or at best, teaching away from the use of the mDC2's of the instant application as vaccines. For example, at page 44 the specification discloses that the mDC2's of the instant claims would promote a Th0/Th2 response and deter a Th1 response. Yet it is well-known in the immunological arts that a Th1 response is critical for the treatment of viral infections and cancers (see for example *Fundamental Immunology*, 1999, Paul,

ed. for a review). At page 48-49, the specification discloses, "One of ordinary skill in the art can readily design a specific vaccination method and strategy for a particular disease or disorder based upon strategies used with conventional mDCl." It is unclear how this assertion can be true (and thus, enabling) given that mDCl induce a Th1 response at the expense of a Th2 response and mDC2 induce a Th2 response at the expense of a Th1 response. Clearly the cells (and methods of use) cannot be considered to be interchangeable. Finally note that the specification at page 49 discloses that the mDC2's of the instant claims can be used as adjuvants and cites *Fundamental Immunology*, 1999, Paul, ed., pages 550-551. A review of the Dendritic Cell chapter in *Fundamental Immunology* reveals that the DCs taught by the reference are DC1's and not the mDC2's of the instant claims. See specifically Figure 8, page 553 which teaches that DC's of the reference are high producers of IL-12, i.e., they are DC1's not DC2's. Accordingly, the use of the mDC2's of the instant invention as a vaccine would be highly unpredictable and requiring of undue experimentation to practice as claimed.

Note that claims drawn to vaccines, i.e., compositions for *in vivo* use, require *in vivo* enablement, or a reasonable correlate, for its intended use. In the instant case, the specification discloses only the induction of a mixed lymphocyte reaction *in vitro*. Said disclosure cannot be considered to be a reasonable correlate for demonstrating the efficacy of a vaccine intended to treat essentially all known pathogen-induced diseases, as well as cancers and autoimmune diseases. The specification provides no working examples demonstrating enablement for any *in vivo* uses of the claimed vaccine. Absent any specific guidance, i.e., working examples, of *in vivo* use, the instant invention would be highly unpredictable and requiring of undue experimentation to practice as claimed.

Regarding Claim 68, the claim recites an mDC that promotes the differentiation of T cells into Th1 cells. The specification discloses that the mDC's of the instant claims promote the differentiation of T cells into Th2 cells. These are essentially mutually exclusive T cell types. Accordingly, an mDC that can induce both Th1 and Th2 differentiation would seem to be highly unexpected and regardless, is not disclosed in the specification. Accordingly, said cells would be highly unpredictable and requiring of undue experimentation to practice as claimed.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples, and the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 33-35, 37-41, 52-59, 68, and 70-76 and are rejected under 35 U.S.C. 102(b) as being clearly anticipated by EP 0808897 (1997, IDS)

EP 0808897 teaches an antigen presenting cell (APC) identified as being devoid of surface CD1a (see particularly page 3, line 11), i.e., a differentiated APC which expresses substantially less CD1a cell surface marker that a conventional dendritic cell. Note that the additional limitations of the claims comprise only further characterization of the claimed cell type, e.g., a cell that substantially lacks IL-12 production. These properties are inherent to the cell of the reference. Some claims, e.g., Claim 38, recite product-by-process limitations, e.g., a differentiated cell cultured in Yssel's medium. Absent a showing that the process results in a novel product, said process is irrelevant. Further note that the source of the cells, i.e., monocyte derived, is also irrelevant absent a showing that said source provides novel properties. In the instant case, no such showing has been made. Accordingly, the cells of the reference are the cells of the instant claims.

The reference clearly anticipates the claimed invention.

11. Claims 33-35, 37-41, 52-59, 68, and 70-76 and are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ito et al. (1999)

Ito et al. teaches an APC identified as being devoid of surface CD1a (see particularly page 1415, column 2, ***Fraction 3*** and ***Fraction 2***). as set forth above, the additional limitations of the claims comprise only further characterization of the

claimed cell type, e.g., a cell that substantially lacks IL-12 production. These properties are inherent to the cell of the reference. Some claims, e.g., Claim 38, recite product-by-process limitations, e.g., a differentiated cell cultured in Yssel's medium. Absent a showing that the process results in a novel product, said process is irrelevant. Further note that the source of the cells, i.e., monocyte derived, is also irrelevant absent a showing that said source provides novel properties. In the instant case, no such showing has been made. Accordingly, the cells of the reference are the cells of the instant claims.

The reference clearly anticipates the claimed invention.

12. Claims 33-35, 37-41, 52-59, 68, and 70-76 and are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Rissoan et al. (1999)

Rissoan et al. teaches an APC identified as substantially lacks IL-12 production that induce Th2 differentiation (see particularly page 1183, column 3, and page 1184, column 3). As set forth above, the additional limitations of the claims comprise only further characterization of the claimed cell type, e.g., being devoid of surface CD1a. These properties are inherent to the cell of the reference. Some claims, e.g., Claim 38, recite product-by-process limitations, e.g., a differentiated cell cultured in Yssel's medium. Absent a showing that the process results in a novel product, said process is irrelevant. Further note that the source of the cells, i.e., monocyte derived, is also irrelevant absent a showing that said source provides novel properties. In the instant case, no such showing has been made. Accordingly, the cells of the reference are the cells of the instant claims.

The reference clearly anticipates the claimed invention.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to

the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 at (703) 305-3014. The CM1 Fax Center telephone numbers are 703-872-9306 (before final) and 703-872-9307 (after final).

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Primary Examiner
Technology Center 1600
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